Our ref: KON-1870 Client's ref: P6388-001-0000 (US)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

----------x

In re Application of: Eiichi UEDA, et al : Art Unit: 1618

Appln. No.: 10/824,095 : Examiner: M.J.

Filed: April 13, 2004 : Perreira

For: LIPOSOME-CONTAINING RADIOGRAPHIC CONTRAST MEDIUM AND PREPARATION METHOD THEREOF :

CONFIRMATION #6153

----------x

DECLARATION

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

S i r:

I, Akihisa NAKAJIMA, hereby declare and say as follows:

1. I am one of the named Inventors in this Application.

2. I graduated from Osaka University in March of 1987 with a Masters Degree in Synthetic Chemistry. Since April of 1987, I have been employed by Konica Corporation, the Assignee of the above-identified Application and have

specifically been engaged in the research and development of photographic material supports.

3. I am aware that the Examiner has suggested providing a comparison of PEGylated liposomes (phospholipid modified with a polyalkylene oxide) of this Application to the liposomes taught in Otake (US 2004/0099976). I am of the opinion that liposomes that include either a phospholipid modified with a polyalkylene oxide or a compound containing a polyoxyalkylene group, results in a surprising and unexpected improvement in an amount of iodine compound encapsulated in the liposome compared to the teachings of Otake. Therefore, tests were performed to compare the amount of iodine included in Otake's liposomes to the amount of iodine included in liposomes made in accordance with this Application with the addition of either a phospholipid modified with a polyalkylene oxide or a compound containing a polyoxyalkylene group.

4. A first encapsulated substance, labeled Sample A, was prepared following the method of Example 4 of Otake as taught on page 4, except that only one phospholipid, dipalmitoylphosphatidylcholine (DPPC) was used; neither ethanol nor magnesium L-ascorbyl phosphased were used; and

an iodine compound (iohexol) in the amount shown in Table 5, attached hereto, was used. The weight percent of the iodine compound in the vesicle is reported in Table 5.

5. A second encapsulated substance, labeled Sample B, was prepared in the same way as Sample A, except that in addition to DPPC, a phospholipid modified with a polyalkylene oxide was added to the initial mixture. The modified phospholipid was distearoylphosphatidylethanolamine covalently bonded to polyethylene glycol, a PEGylated liposome (DSPE-O2OCN available from NOF Corporation). The weight percent of the iodine compound in the vesicle is reported in Table 5.

6. A third encapsulated substance, labeled Sample C, was prepared in the same way as Sample A, except that in addition to DPPC, a compound containing a polyoxyalkylene group, PLURONIC F-88 (a block copolymer of polyethylene oxide and polypropylene oxide available from ADEKA CO.) was added to the initial mixture. The weight percent of the iodine compound contained in the vesicle is reported in Table 5.

7. The determination of the amount of iodine compound contained in the vesicle was determined in the same manner as disclosed in the Application, see page 43, line 17.

8. As can be seen in Table 5, the amount of iodine compound in the vesicle in Samples B and C was greater than the amount of iodine in the vesicle of sample A by a factor of 1.5 to 2. It is surprising and unexpected that the amount of iodine in Samples B and C is greater than Sample A.

9. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under 18 USC 1001 and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Akihisa Nakajima
Akihisa NAKAJIMA

Dated: This 17th day of November 2008.

DCL/mr
Attached: Table 5

Table 5

Sample	method of preparing a liposome	substance to be encapsulated	substance to be mixed with a phospholipid	propotion (weight percentage of iodine compound included in vesicles based on total iodine compound)	Remarks
A	the Example 4 of Otake, except no ethanol was used	647 mg/ml of iohexol (300mgI/mL)	none	13%	Comparative
B	the Example 4 of Otake, except no ethanol was used, further a phospholipid modified with a polyalkylene oxide was mixed	647 mg/ml of iohexol (300mgI/mL)	a phospholipid modified with a polyalkylene oxide (DSPE-020CN, available from NOF CORPORATION)	25%	Inventive
C	the Example 4 of Otake, except no ethanol was used, further a compound containing a polyoxyalkylene group was mixed	647 mg/ml of iohexol (300mgI/mL)	a compound containing a polyoxyalkylene group (pluronic F-88, available from ADEKA Co.)	20%	Inventive